

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau



69 JUL 2004



(43) International Publication Date
12 June 2003 (12.06.2003)

PCT

(10) International Publication Number
WO 03/048154 A1

(51) International Patent Classification⁷: **C07D 401/12**,
401/14, 471/04, A61K 31/4709, A61P 09/02

VELKER, Jörg [DE/DE]; Stadionstrasse 1, 79539 Lörrach (DE). **WELLER, Thomas** [CH/CH]; Hoelzlistrasse 58, CH-4102 Binningen (CH).

(21) International Application Number: **PCT/EP02/13577**

(22) International Filing Date: 2 December 2002 (02.12.2002)

(74) Agent: **HOFMANN, Dieter**; StratAll, Therwilerstrasse 87, CH-4153 Reinach (CH).

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
PCT/EP01/14195 4 December 2001 (04.12.2001) EP

(71) Applicant (for all designated States except US): **ACTELION PHARMACEUTICALS LTD** [CH/CH]; Gewerbestrasse 16, CH-4123 Allschwil (CH).

(72) Inventors; and

(75) Inventors/Applicants (for US only): **AISSAOUI, Hamed** [FR/FR]; 01, Rue du Vieil Armand, F-68270 Wittenheim (FR). **BINKERT, Christoph** [CH/CH]; In den Ziegelhoeften 89, CH-4054 Basel (CH). **CLOZEL, Martine** [FR/CH]; Winterhalde 3b, CH-4102 Binningen (CH). **MATHYS, Boris** [CH/CH]; Baumgartenstrasse 839, CH-4622 Egerkingen (CH). **MUELLER, Claus** [DE/FR]; 4, rue de Buschwiller, F-68220 Hegenheim (FR). **NAYLER, Oliver** [CH/CH]; Brädmattstrasse 1, CH-4144 Arlesheim (CH). **SCHERZ, Michael** [US/CH]; Schaiengaessli 2, CH-4107 Ettingen (CH).

(81) Designated States (national): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.

(84) Designated States (regional): ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Published:

— with international search report

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: 4-(PIPERIDYL- AND PYRROLIDYL-ALKYL-UREIDO) -QUINOLINES AS UROTENSIN II RECEPTOR ANTAGONISTS

(57) Abstract: The invention relates to novel 1-pyridin-4-yl urea derivatives and related compounds and their use as active ingredients in the preparation of pharmaceutical compositions. The invention also concerns related aspects including processes for the preparation of the compounds, pharmaceutical compositions containing one or more of those compounds and especially their use as neurohormonal antagonists.



WO 03/048154 A1

INTERNATIONAL SEARCH REPORT

 International Application No.
 PCT/EP 02/13577

 A. CLASSIFICATION OF SUBJECT MATTER
 IPC 7 C07D401/12 C07D401/14 C07D471/04 A61K31/4709 A61P09/02

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 C07D

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the International search (name of data base and, where practical, search terms used)

EPO-Internal, WPI Data, PAJ, BIOSIS, CHEM ABS Data, BEILSTEIN Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	WO 01 45700 A (KNIGHT STEVEN DAVID ; SMITHKLINE BEECHAM CORP (US); WIDDOWSON KATHE) 28 June 2001 (2001-06-28) cited in the application claims 1,5	1-27
A	WO 01 45711 A (KNIGHT STEVEN DAVID ; SMITHKLINE BEECHAM CORP (US); DHANAK DASHYANT) 28 June 2001 (2001-06-28) cited in the application claims 1,4	1-27

☐ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

* Special categories of cited documents:

- *A* document defining the general state of the art which is not considered to be of particular relevance
- *E* earlier document but published on or after the international filing date
- *L* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- *O* document referring to an oral disclosure, use, exhibition or other means
- *P* document published prior to the international filing date but later than the priority date claimed

- *T* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- *X* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- *Y* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- * & * document member of the same patent family

Date of the actual completion of the international search

27 February 2003

Date of mailing of the international search report

05/03/2003

Name and mailing address of the ISA

 European Patent Office, P.B. 5818 Patentlaan 2
 NL - 2280 HV Rijswijk
 Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,
 Fax: (+31-70) 340-3016

Authorized officer

Seelmann, I

INTERNATIONAL SEARCH REPORT

Internal application No

PCT/EP 02/13577

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
WO 0145700	A	28-06-2001	EP 1246619 A1	09-10-2002
			WO 0145700 A1	28-06-2001
			US 6514970 B1	04-02-2003
WO 0145711	A	28-06-2001	EP 1244452 A1	02-10-2002
			WO 0145711 A1	28-06-2001

INTERNATIONAL SEARCH REPORT

International application No.

PCT/EP 02/13577

A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 C07D401/12 C07D401/14 C07D471/04 A61K31/4709 A61P09/02

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 C07D

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the International search (name of data base and, where practical, search terms used)

EPO-Internal, WPI Data, PAJ, BIOSIS, CHEM ABS Data, BEILSTEIN Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	WO 01 45700 A (KNIGHT STEVEN DAVID ;SMITHKLINE BEECHAM CORP (US); WIDDOWSON KATHE) 28 June 2001 (2001-06-28) cited in the application claims 1,5	1-27
A	WO 01 45711 A (KNIGHT STEVEN DAVID ;SMITHKLINE BEECHAM CORP (US); DHANAK DASHYANT) 28 June 2001 (2001-06-28) cited in the application claims 1,4	1-27

☐ Further documents are listed in the continuation of box C.☒ Patent family members are listed in annex.

* Special categories of cited documents:

- *A* document defining the general state of the art which is not considered to be of particular relevance
- *E* earlier document but published on or after the international filing date
- *L* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- *O* document referring to an oral disclosure, use, exhibition or other means
- *P* document published prior to the international filing date but later than the priority date claimed

T later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

X document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

Y document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

8 document member of the same patent family

Date of the actual completion of the international search

27 February 2003

Date of mailing of the international search report

05/03/2003

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2
NL - 2280 HV Rijswijk
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,
Fax: (+31-70) 340-3016

Authorized officer

Seelmann, I

INTERNATIONAL SEARCH REPORT

Internationa Application No
PCT/EP 02/13577

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
WO 0145700	A	28-06-2001	EP 1246619 A1	09-10-2002
			WO 0145700 A1	28-06-2001
			US 6514970 B1	04-02-2003
WO 0145711	A	28-06-2001	EP 1244452 A1	02-10-2002
			WO 0145711 A1	28-06-2001